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EXAMINER

REYES, HECTOR M

ART UNIT PAPER NUMBER

1625

DATE MAILED: 03/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/075,442

Applicant(s)

NEOGI ET AL.

Examiner

Hector M Reyes

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25 to 30, 47 to 50 and 67 to 71 is/are pending in the application.
- 4a) Of the above claim(s) 28-30, 49, 50, 69 and 70 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 25, to 27, 47, 48, 67, 68 and 71 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: _____

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DETAILED ACTION

Paper Entry

Examiner acknowledges Applicant's Amendment filed on December 24, 2002 as paper no. 6.

Status of The Claims

Claims 25 to 30 47 to 50 and 67 to 71 are pending in the instant application.

Claims **28 to 30, 49, 70, 50 and 69** are withdrawn from consideration as ***properly indicated in the Office Action Summary of the previous Office Action, Paper no. 5.*** Currently, claims 25-27, 47, 48, 68 and new claim 71 are under Examination.

Specification

Examiner acknowledges Applicant's darker copy of the specification directed to overcome the specification's objection of the previous Office Action. Such copy is indeed much in much better conditions that the first copy received on the record.

Rejection of Claims 25 to 27; 47, 48 and 67 to 68 under 35 USC 112, first paragraph is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 25 to 27; 47, 48 and 67 to 68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the

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specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In Claim 25, Applicants claim an extensive list of compounds, having the general formula II. The method of preparation of such compounds, however, is not described anywhere in the specification. Regarding such preparation, in page 9 of the specifications it is said "A specific method for the synthesis of a representative number of compounds of the formula I is shown below in Scheme IA. *Compounds of the formula II where made starting from the second step showing in Scheme I with the appropriate starting materials.* Such limited sentence in reference to a general Scheme is insufficient to describe a proper preparation of the claimed compounds in such a way that enable one skill in the art to make such extensive number of compounds without undue experimentation. The factors to considering in determining the required undue experimentation are, among others:

- The breadth of the claim
- The nature of the invention
- The state of the art
- The level of one of ordinary skill
- The level of predictability in the art
- The amount of direction provided by the inventor
- The existence of working examples

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- The quantity of experimentation needed to make or use the invention based on the content of the disclosure see discussion of *In re Wands* 858 F2d 731, 737, 8 USPQ2d1400, MPEP 2164.01 and 2164.01(a).

In this particular case,

- Claim 25 embraced a quite extensive groups of compounds as can be deduced by the extensive groups that can satisfied the 10 variables moieties present in the said general formula;
- The specification lacks a disclosure of at least one working example describing the preparation of any of the compounds embraced by formula II
- In the organic synthesis art, the preparation of a given compound require to follow an specific sequence of steps and to control a variety of conditions in order to successfully prepared such compounds. Such reaction conditions are needed because it is unpredictable if a given starting material under a given and particular reactions conditions will eventually produce a wanted target. Conditions such as mixing order, initial temperature, pressure, time, etc should be at least define to certain and considerable extend, in such a way that a person skill in the art can reproduce the synthetic procedure without undue experimentation.
- In this particular case the only disclosure directed to the synthesis of the claimed compounds is a general reference to a general Scheme, without providing even one example of the required synthetic

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procedure for the preparation of specie within the broad claimed genus. Moreover, in the specification, page 1, first sentence, the novelty of such derivatives is disclosed, since is said, "the present application is directed to novel antidiabetic compounds. Therefore, there should not be any disclosed method in the art that can allow a person skilled in the art to prepare such derivatives.

- In the absence of such procedure, extensive experimentation directed to find the proper reactions conditions in the preparation of any compound embraced in such extensive list of claimed is required. Moreover, the finding of proper conditions in the preparation of the most simple species does not warranty that the same conditions could be used in the preparation of other more complicated structures, for example, in compounds having multiple substituents with a variety of functionalities which may required protection and de-protection or specific and particular reactions conditions. The preparation of pharmaceuticals preparations or any method of use the claimed compounds are other aspects of the instant invention. However, if the claimed derivatives cannot be synthesized, then such aspects of the instant invention are affected because without the compounds, their method of use or the preparation of compositions comprising the same cannot be achieved.

Rejection of Claims 25 to 26 under 35 USC 112 are hereby maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear which of the periods found in claim 25 finalized the description of the claimed invention. There is a total of four periods on the claim: after the letter H and after the word alkylcarboxylamino in the B and B' variable definition, after the word cyano in the R groups definition and after the SO₂ group in the X group definition. In claim 26, there is a total of two periods: after the word cyano and after the SO₂ group in the X definition. Please see section 608.01(m) of the MPEP, wherein had been point out that ***"Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations"***.

Claims 25, 26 27, 47, 48, 67 and 68 are unclear. While in such claim, the variables At, Bx, Cw, Au and By are defined as substituents on any position of the specific ring, the values of t, u, y, x and w are defined as 0 to 3. Therefore, such definition includes those compounds wherein the variables groups A, B and C or A' and B' are not present in the ring since the value of t, u, y, x and w can be zero. Hydrogen is included within the definition of A, A' B, B' and C groups and therefore excluded as a possibility when all the variables t, u, y, x and w are 0. In such instances, it is not indicated which substituents are found in any of the rings and therefore in such case the definition of the claimed compounds is indefinite.

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Definition of the substituents on the ring when t, u, y, x and w are zero is required in order to clarify both claims.

Previous Rejection of Claims 25, 27, 47, 48, 67 and 68 are hereby modified in view of Applicant's Amendment of the Claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Kummer et al, US patent 4,110,470.

Kummer discloses:

- A series of compounds having the general formula 1, as described in column 2, lines 24 to 62 and its intermediates as described for instance in col. 6 and 7.
- Its method of preparation as detailed on columns 3, 4, 5 and 6 and in the pertinent examples 1 to 9
- Pharmaceutical preparations comprising such derivatives as described in example 10 to 11,

Kummer also discloses that such derivatives are especially noteworthy for they lipid-controlling including their cholesterol-controlling properties, such as lowering

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the level of cholesterol and also of triglycerides in warm-blooded animals. These properties were confirmed in clinical work on patients suffering from diabetes and in other patients suffering other related diseases (see col. 14, lines 39 to 52).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 25, 26, 27, 47, 48, 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kummer et al, US patent 4110470.

Kummer discloses:

- A series of compounds having the general formula 1, as described in column 2, lines 24 to 62,
- Its method of preparation as detailed on columns 3, 4, 5 and 6 and in the pertinent examples 1 to 9

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- Pharmaceutical preparations comprising such derivatives as described in example 10 to 11,

Kummer also discloses that such derivatives are especially noteworthy for they lipid-controlling including their cholesterol-controlling properties, such as lowering the level of cholesterol and also of triglycerides in warm-blooded animals. These properties were confirmed in clinical work on patients suffering from diabetes and in other patients suffering other related diseases (see col. 14, lines 39 to 52).

Kummer discloses iodine derivatives but do not discloses other analogs halogens as chorine, bromine or fluorine derivatives.

The preparation of analogs halogen derivatives wherein a iodine atom is change by any other halogens in order to be used to the same intended use results obvious to a person skill in the art.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25, 26, 27, 47, 48, 67, 68 and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 71 is directed to ***a compound of claim 1***. Such claim has been already canceled by preliminary amendment and therefore is directed to subject matter foreign to the claimed subject matter.

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In claim 25, 26, 27, 47, 48, 67 and 68 variables groups:

- A, A' and C
- B and B'
- R', R" and R''' and
- X

are defined as being independently a series of different functional groups, which are quite different. Such definition is indefinite because it is impossible that variable group could be simultaneously all of the described possibilities.

Examiner suggests that such definition is described as possibilities. For instance, a phrase indicating that such variable groups "are independently selected from a groups consisting of"....before the series of possible functional groups would supply the lack of clarity and definition.

In claims 25, 26, 27, 47, 48, 67 and 68 the alkenyl option of variable groups R', R" and R''' are said to "may contain substituents. However, there is a clear lack of definition because no definition of the said substituents is provided.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Gapinski, US patent 4, 996, 230, chemical abstract 115:135918 or Pattner, US patent 4,389416 or Marshall.

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Gapinski discloses a series of tricyclic compounds useful in leukotriene antagonists and its preparation. See derivative II as described in the said abstract.

Plattner discloses a series of compounds having two phenyl structures linked by a oxygen, sulfur, or sulfoxide, useful in hypertension, edema, cardiac failure and other conditions involving fluid and electrolyte accumulation see col. I for the general description and specific compounds embraced by claim 25 through US patent 4,389,416.

Marshall discloses a series of substituted phenyl derivatives directed to treat a series of conditions produced by inflammation. See columns I, 2 and 3.

Claims 25, 47, 48, 67 and 68 are rejected under 35 USC 102 (b) as being anticipated by Dygos et al, *Journal of Medicinal Chemistry*, 1977, vol. 20, n0.12, pp1705.

✓ Dygos discloses a series of biphenyl derivatives having hypocholesterolemic activity. Such compounds derivatives having the ability to reduce serum cholesterol levels and serum triglycerides levels.

Response to Applicants Remarks

On page 9, second paragraph, under Remarks presented by Applicants together with the Amendment, Applicants pointed out that "Preliminarily, it is noted although not noted on the cover sheet to the Official Action, that claim 70 is similarly withdrawn from consideration as it was not elected in response to the restriction requirement." However, a copy of the said action and more specifically

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of the said Office Action Summary is on the record. It is clearly indicated in such Summary, even more specifically, in the 4a section that claims 28-30, 49, **70**, 50 and 69 are withdrawn from consideration. Examiner hereby responds that all claims withdrawn from consideration are properly enumerated in the corresponding section of the previous office action. Please review information on Summary Action again in order to verify the issue. Nevertheless, the said claim 70 is indeed withdrawn from consideration as already properly indicated.

Rejection of claims 25, 27, 47- 48 and 67 under 35 USC 112 first paragraph

Regarding the rejection base upon the lack of enablement Applicant had argued that:

- One skill in the art could readily practice the claimed invention with the teaching offered in the specification.

Such argument has been fully considered, however the generality of the description found in the specification had already been discussed by the examiner as one of the In re Wands factors discussed in and enablement are not equivalent terms. On the other hand, if as indicated in the said argument a person skill in the art can practice the invention base upon a general description and a clear lack of enablement, then the said invention lacks novelty because practically, the said invention is within the knowledge of those skilled in the art. Moreover, essential elements required to used and practice the invention as starting materials, reactions conditions and other already discussed in the previous office action are not even identified. Without such essential elements how the invention can be practice, for example how the thousand or million of

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compounds embraced by claim 25 can be properly prepared in order to further used them in any possible method?

Rejection under 35 USC 112 second paragraph

Regarding the said rejection, Applicant's argued that:

- Claim 25 and 26 are clear and in full compliance with the 35 USC 112 and that the expected visual differences between commas and periods are now clearly apparent
- Claims 25-27, 47, 48 and 67-68 are clearly defined because by long standing convention, both in the field of chemistry and adopted in the field of patent law, the presence of the hydrogen atoms are implied when drawing chemical structures

Regarding the issue of clarity and compliance with the second paragraph,

Applicant attention is once again brought to the fact that:

- It is unclear which of the periods found in claim 25 finalized the description of the claimed invention. There is a total of four periods on the claim: after the letter H and after the word alkylcarboxylamino in the B and B' variable definition, after the word cyano in the R groups definition and after the SO₂ group in the X group definition. In claim 26, there is a total of two periods: after the word cyano and after the SO₂ group in the X definition.
- A claim having multiple periods is far from compliance with the required clarity required under the second paragraph of 35 USC 112.

Regarding the lack of definition in the substituents of the claimed compounds and more specifically by the inclusion of hydrogen in the groups of substituents it is

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unclear what substituents are present if even hydrogen is banned to be present.

Examiner agrees that hydrogen's atoms presence is implied when drawing chemical structures. However, that is not the base of the rejection. The point is that a given variable cannot be defined as simultaneously be hydrogen and at the same time as being not hydrogen. Such possible definition lacks clarity and is indefinite.

In order to further clarify the said claims more specific rejections are hereby present.

Rejection of claims 25, 27, 47, 48, and 67-68 under 35 USC 102

Applicant traverse the said rejection and argued requested it should be withdrawn in view of Applicant's amendment.

Applicant's amendment is directed to change the substituent "halogen" by the substituents bromo chloro and fluoride, eliminating the possibility of having iodine as a substituent.

The Examiner wants to point out that Applicant did not consider other compounds present in the said reference and used as intermediates as for example compounds XIV and XVIII, for example. Such compounds are also embraced in claim 25 and are not overcome by the said amendment because they have no iodine as substituent.

Moreover, Applicant's amendment open the door for a prima facie case of obviousness because of the interchange of a halogen substituent, such as iodine by another halogen, such as -bromo, chloro or fluoride in the same general

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structure, directed to the same utilities is an obvious matter. The present modification of the said rejection is hereby directed to these aspects.

THE PRESENT REJECTION

The present action is not final. The Examiner want to clearly indicates on the record that an extensive list of references embracing the claimed compounds described in claim 25 had been obtained as a result of an official prior art search. Because of the fact that it is not practical nor it is necessary, only a few references had been included in the rejection of such claim.

CONCLUSION

Any inquiry concerning this communication should be directed to Hector M. Reyes whose telephone number is (703) 605-1153. The examiner can normally be reached on Monday to Friday from 8am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner 's supervisor, Allan Rotman can be reached on (703) 308-4698. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556 or for regular communication and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



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